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Care for bipolar disorder in LMICs needs evidence from local settings

Bipolar disorder is eminently treatable, however, treatment guidelines developed in low-income countries barely mention treatment of bipolar disorder, and the treatment gap for this disorder is substantial: 75% in middle-income countries,[1] 90% in Ethiopia,[2] and nearly 100% if prophylactic rather than acute-phase treatment is considered. Bipolar disorder is at risk of being left further behind as integrated mental health care is scaled up worldwide. One reason is the absence of data: the psychopathology, incidence, prevalence, and course of bipolar disorder are poorly described in low-income and middle-income countries (LMICs). Another reason is a misplaced emphasis on evidence-based treatments in the absence of contextualised evidence.

According to the Mental Health Gap Action Programme intervention guide (mhGAP-IG),[3] the preferred treatments for both acute and prophylactic phases of bipolar disorder are classic mood stabilisers (lithium, valproate, and carbamazepine). Even though the mhGAP-IG recommends the possible use of antipsychotic drugs, such as haloperidol, in the acute management of bipolar disorder, it offers no such alternatives for prophylactic treatment. Antipsychotic are often used in mania[4] and are continued over many months even after the acute phase has improved. Depot first-generation antipsychotic drugs[5] and other first-generation antipsychotic drugs[2] have been in

use to treat bipolar disorder, with some evidence of benefit in naturalistic studies. No adequately powered, randomised studies support the conclusion that typical antipsychotic drugs worsen bipolar depression, but these are the treatments that are widely available in LMICs. Even when mood stabilisers and atypical antipsychotic drugs are available in some tertiary centres, their availability is intermittent and unpredictable. The system features of primary health- care services in most LMICs make it impossible to use mood stabilisers safely in those settings.

A further complication with reliance on classic mood stabilisers is that women of reproductive age form a higher percentage of the population in LMICs than in high-income countries. At the same time, women in LMICs have poorer access to effective forms of contraception, thus enhancing the population-level risk of teratogenicity from mood-stabiliser exposure during pregnancy. Current guidelines for bipolar disorder are therefore inequitable, excluding most women in LMICs.
Indeed, owing to the non-availability of the necessary system requirements, human resources, and medications at the primary-care level, if the existing guidelines are adhered to rigidly, they have the potential to worsen the treatment gap for bipolar disorder. The absence of feasible recommendations for prophylactic treatment in LMICs leaves a large population of patients with a severe but treatable disorder without options. This is a clear gap that has to be addressed urgently.

Alternative methods to obtain evidence—eg, so- called practice-based approaches, despite potential limitations—are needed as short-term options to bridge the gap between what we desire for treatment of bipolar disorder and what could be feasibly implemented. This complementary form of evidence draws on the experience of service users, caregivers, and health workers who have accumulated expertise in the management of health conditions in real-life settings.[6] For example, many psychiatrists in LMICs have been managing bipolar disorder for decades and have relied on

first-generation antipsychotic medication for both acute and prophylactic treatment, despite the absence of rigorous randomised controlled trials investigating this approach. Evidence could be gathered from these psychiatrists about feasible options for prophylactic treatment. This proposal is not to advocate second-rate treatment for patients in LMICs. On the contrary, it is about advocating treatment that is likely to be feasible in the short term. The alternatives are either patients not receiving any treatment or patients not receiving best possible evidence-based treatment. At the same time as using practice-based evidence for immediate care provision, it is essential to expand access to mood-stabilisers in LMICs and develop health systems to support their safe and effective use. In view of the complexity of bipolar disorder and its management, advocacy should be made not only for scale-up of integrated care but also for scale-up of specialist care.

Any guideline should consider whether the recommended treatments benefit women and the poor equally. Consideration needs to be given to the potential role of second-generation antipsychotic medications[7] with mood-stabilising properties because they seem to be safer in pregnancy and are more straightforward to prescribe than first-generation antipsychotic drugs. Moreover, these second-generation drugs can treat and prevent many manifestations of the illness (including depressed, manic, mixed, and psychotic states), and are increasingly affordable with the emergence of generic preparations. The prophylactic treatment of bipolar disorder is associated with substantial costs. Treatment options that are affordable or otherwise subsidised are essential. Finally, in the long term, a pressing need is to develop an evidence base of treatment for bipolar disorder that is informed by cost-effectiveness trials in primary-care settings in LMICs.

Evidence on psychosocial interventions is similarly sparse in LMICs. The mhGAP-IG recommends brief education-based interventions for relapse prevention, but the effectiveness of these brief

interventions in primary-care settings and in LMICs is not supported by evidence. Beneficial psychological treatments, even in the early phases of the illness, have included approaches that are more complex and that need careful adaptation, such as cognitive behavioural therapy, interpersonal therapy, and individual, family, and group psychoeducation.[8,9] Implementation of components of cognitive behavioural therapy by lay health-care providers has been shown to be feasible in LMICs.[10,11] Such interventions could be delivered in primary-care settings. Family-based psychoeducation approaches delivered by lay health workers could also be explored, because most patients in LMICs visit health facilities with their families. Combining these psychosocial interventions with first- generation antipsychotic drugs could offset the inability of these drugs to prevent relapses of the depressive cycles of bipolar disorder. Clinical studies need to establish evidence regarding the benefit of these simple interventions and whether they could potentially be administered by lay health workers. Patients with bipolar disorder are already poorly served by health-care systems in LMICs: they must not be left further behind through inappropriate investment in mental health services.

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